## natureresearch

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## Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see <u>Authors & Referees</u> and the <u>Editorial Policy Checklist</u>.

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For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a Confirmed
The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
The statistical test(s) used AND whether they are one- or two-sided  Only common tests should be described solely by name; describe more complex techniques in the Methods section.
A description of all covariates tested
A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. means) or other basic estimates (e.g. regression coefficient)
Give P values as exact values whenever suitable.
For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
Estimates of effect sizes (e.g. Cohen's d, Pearson's r), indicating how they were calculated
Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.
Software and code
Policy information about <u>availability of computer code</u>
Data collection The data that support the findings of this study are available from MR-Base (www.mrbase.org)
Data analysis  All analyses were conducted with the TwoSampleMR package of MR-Base (https://github.com/MRQIEU/TwoSampleMR) and the MR-TRYY package (https://github.com/explodecomputer/tryx) in 8 statistical software (ver 3.4.1).
for manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GilHiub). See the Nature Research <u>nucleines for submitting code &amp; software</u> for further information.
Data

## Field-specific reporting

The data that support the findings of this study are available from MR-Base (www.mrbase.org).

lease select the one below	v that is the best fit for your research	If you are not sure, read the appropriate sections before making your selection
Life sciences	Behavioural & social sciences	Ecological, evolutionary & environmental sciences

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets

- A list of figures that have associated raw data

- A description of any restrictions on data availability

## Life sciences study design

All studies must disclose on these points even when the disclosure is negative.		
Sample size	Sample size should be over 5,000 but can vary depending on the size of the original GWA study.	
Data exclusions	We excluded GWAS results registered at MR-Base have less than 500,000 SNPs and sample sizes less than 5,000.	
Replication	N/A	
Randomization	N/A	
Blinding	N/A	

We require information from authors about some types of materials, e	experimental systems and methods used in many	studies. Here, indicate whether each mate
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Blinding N/A		
Reporting for	specific materials, systems and methods	
	thors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, and to your study, if you are not sure if a list item applies to your research, read the appropriate section before selecting a response.	
Materials & experimen	tal systems Methods	
n/a Involved in the study	n/a Involved in the study	
Antibodies	ChiP-seq	
Eukaryotic cell lines	⊠ Flow cytometry	
	MRI-based neuroimaging	
Animals and other ora	— <del>-</del> -	
Human research parti	cipants	
Clinical data		
Human research p	articipants	
Policy information about stu	dies involving human research participants	
Population characteristics	N/A	
Recruitment	N/A	
Ethics oversight	The present study is exempted from ethical consideration since we only used secondary data (summary statistics) which are publicly available.	
Note that full information on the	approval of the study protocol must also be provided in the manuscript.	
Clinical data		
Policy information about clin	ical studies	
All manuscripts should comply w	$ith \ the \ ICMJE \ \underline{guidelines \ for \ \underline{publication \ of \ clinical \ research}} \ and \ a \ completed \ \underline{CONSORT \ checklist} \ must \ be \ included \ with \ all \ submissions.$	
Clinical trial registration	N/A	
Study protocol	N/A	
Data collection	N/A	